PSORIAMED®

PSORIAMED®

LE CONCEPT D'APPAREIL INNOVATEUR POUR UNE THÉRAPIE EFFICACE DU PSORIASIS

PHYSIOMED®
ELEKTROMEDIZIN

TECHNOLOGY FOR THERAPY

PSORIAMED®

PSORIAMED® est un appareil cliniquement testé, basé sur les exigences d'une thérapie à action rapide, mais facile à utilisation car nécessitant l'application de courants de stimulation.

Sans irriter les zones affectées, les courants d'interférence IFS traversent en douceur les barrières de résistance de la peau et agissent ainsi sur les zones présentant cette dysfonction. L'effet antipsoriasique de l'IFS est basé sur la normalisation des processus de division cellulaire ainsi que sur une action anti-inflammatoire et anti-oedémateuse.

Grâce à la transmission d'informations appropriées, stimulant ainsi le métabolisme cellulaire, le temps de traitement avec PSORIAMED® est de courte durée, d'une intensité faible et agréable. L'efficacité de ce traitement, dont l'inocuité est totale, est une alternative et, ou un adjuvant au traitement du psoriasis.

Pour obtenir des bons résultats, le traitement doit être réalisé deux fois par jour (le matin et le soir). On peut appliquer les courants de stimulation soit dans un bain d'eau, soit à l'aide d'électrodes spéciales.

Pour le traitement, le menu de l'appareil offre des propositions de thérapie préprogrammées, ainsi que des graphiques. Grâce à son écran graphique clair et à sa modulation à l'aide d'un seul potentiomètre, PSORIAMED® est un appareil extrêmement facile à utiliser. Pour les applications dans des bains d'eau, l'appareil est pourvu d'un interrupteur à pédale pour régler sans problème l'intensité du courant. Le fonctionnement avec une batterie rechargeable garantit la sécurité d'utilisation de l'appareil et permet de s'en servir lors de déplacements.

Ecran à ordre clair avec images de traitement

Commande au pied
(optionnel)

Pour opération sûre et confortable pendant le traitement.

DONNÉES TECHNIQUES :

Puissance d. sortie maxi.:	100 mA/500 Ohm
Puissance:	25 VA
Tension nominale:	100–240 V
Classe de protection:	1, type BF
Dimensions (L x H x P):	315 x 104 x 285 mm
Poids:	3,1 kg

ACCESSOIRES STANDARD :
2 Coupes de traitement
2 Electrodes flexo EF 400
2 Sachets en viscose EF 400
10 Grilles à distance
2 Rubans textiles élastiques 10 x 125 cm
1 Câble de patient (bipolaire)
1 Câble d'alimentation
1 Mallette de transport
1 Mode d'emploi
1 Dossier thérapeutique „Psoriasis"

ACCESSOIRES SUPPLÉMENTAIRES :
Commande au pied
Electrode spéciale (bras)
Electrode spéciale (tête)
Câble de liaison avec serre-fermoir (jeu de 2)
Electrode flexo EF 200 (jeu de 2)
Sachet en viscose EF 200
Chariot *Universal II*

Tous les appareils PHYSIOMED se conforment aux dernières normes de sécurité et de fabrication en vigueur. Ils sont fabriqués selon les normes standard d'assurance qualité et passent les tests type leur permettant d'obtenir le marquage CE obligatoire de la Directive 93/42 CEE.

Demandez nos offres de location intéressantes !

TECHNOLOGY FOR THERAPY

CE 1275

Geprüfte Qualitätssicherung

ISO 9001

MADE IN GERMANY

08/2006 Spécifications et design susceptibles d'être modifiés sans avertissement préliminaire.

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Quel est le mode d'action de PSORIAMED® ?

Le traitement cellulaire agit spécifiquement sur les cellules qui présentent une anomalie fonctionnelle. On sait depuis longtemps que le taux d'adénosine monophosphate cyclique (AMP cyclique), un messager de notre organisme, est considérablement plus faible dans les cellules cutanées psoriasiques que dans des cellules normales. DERTINGER et ses collaborateurs ont pu montrer dans des études de biologie cellulaire que ce messager cellulaire peut être stimulé de façon ciblée par l'application de courants de stimulation à fréquence moyenne.

Des « fenêtres de fréquences » précises ont révélé une efficacité optimale dans les tests cliniques. Ces études ont non seulement mis à jour une élévation du taux d'AMP cyclique, mais également une augmentation de la synthèse de l'interleukine 10, une cytokine anti-inflammatoire. L'efficacité antipsoriasique élevée de ce traitement s'explique aussi bien par la normalisation de la division cellulaire des kératinocytes, que par une action anti-inflammatoire et anti-œdémateuse.

Étude de cas pratique

Diagnostic : Psoriasis sur la paume depuis environ 2 ans
Traitement : Arrêt du traitement précédent 14 jours avant le traitement par PSORIAMED®; deux séances quotidiennes de 5 minutes, matin et soir.

Début du traitement

20 jours après

Fin du traitement

Le concept thérapeutique PSORIAMED® est également disponible en location !

PHYSIOMED®
ELEKTROMEDIZIN
www.soulager-le-psoriasis.fr

Erreurs réservées. Spécifications et design susceptibles d'être modifiés sans avertissement préliminaire. 06/2007

Une nouvelle solution pour le psoriasis

PSORIAMED®:
Traitement efficace par l'application de courants de stimulation

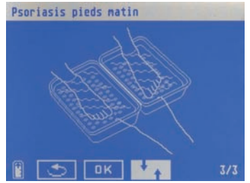
traitement non agressif
sans effets secondaires
testé cliniquement

Vous souffrez de psoriasis ? Dans 90 % des cas, le traitement par PSORIAMED® contribue à une rémission totale ou à une nette amélioration des symptômes !

Concept thérapeutique PSORIAMED®

PSORIAMED® est un concept thérapeutique très facile à utiliser. Les options préprogrammées assurent la rapidité des séances de traitement. Après avoir choisi la zone à traiter, il vous suffit de régler l'intensité, et le traitement commence. Le traitement doit être suivi tous les jours, par deux séances de 5 minutes matin et soir.

Pour le traitement des zones les plus couramment touchées, on utilise des bains d'eau et différentes électrodes spécialement conçus. En plus de ces traitements spéciaux pour les mains, les pieds, les coudes, les bras et la tête, cette méthode peut également être utilisée sur toutes les autres parties du corps grâce aux électrodes flexibles qui s'appliquent à l'aide d'un ruban auto-agrippant.



PSORIAMED® est efficace !

Traitement efficace par l'application de courants de stimulation

Pourquoi l'application de courants de stimulation ?

L'application de courants électriques est considérée comme un mode de traitement efficace et éprouvé. Elle connaît actuellement un regain de popularité grâce à son absence d'effets secondaires. Il n'est pas rare que des patients chroniques ou des patients ayant, en vain, suivi tous les traitements existants développent un nouvel intérêt pour cette option thérapeutique. Dans le traitement du psoriasis aussi, les courants de stimulation présentent des résultats excellents et rapides. Ce traitement se fonde sur un concept thérapeutique développé au centre de recherche de Karlsruhe, en Allemagne, sous la direction du professeur Hermann DERTINGER, et il repose également largement sur des preuves scientifiques. Des études cliniques ont montré l'efficacité élevée de ce traitement, même dans les cas de patients jusque là résistants à toute forme thérapeutique: environ 90 % des patients réagissent à ce traitement non agressif et sans effets secondaires.

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Interferential current is effective in palmar psoriasis: an open prospective trial

Interferential current (IFC) has been shown to improve psoriasis in a small case series. So far no formal clinical trial had been conducted. As IFC is associated with slight prickling sensations a blinded study design was not feasible. Therefore, an open type prospective study was conducted with the assumption of 18% spontaneous remission rate. A response rate of 50% or less was judged as indicating no effect (hypothetical control), while 80% or more was considered as success (alternative hypothesis). In this "quasi-controlled" study 12 patients with therapy resistant palmar psoriasis received local treatment with IFC during a 12 week period. Treatment was performed at low current density in two daily sessions, each of 6 minutes duration. Erythema, scaling, induration, fissures and pustules were recorded in separate scores every 4 weeks. Response of a patient was judged positive when the total score of these criteria was reduced at least by two points at the end of treatment. After 12 weeks of treatment, 11 of 12 patients were cured or showed marked remission with the median overall score reduced by 4 points. An interim analysis was performed in order to decide whether the results had already reached significance ($a < 0.05$). The analysis revealed a statistically significant response rate of 90% (95% confidence interval 62-99%). These results arc highly encouraging and should focus attention on this new therapy modality, which, in contrast to other treatments is not associated with side effects and discomfort. *(Key words: psoriasis, interferential current, clinical trial, shifted null hypothesis.)*

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Palmoplantar psoriasis is a disabling condition which is very difficult to treat [1]. It is usually resistant to most of the available therapeutic modalities like topical glucocorticosteroids, vitamin-D derivates and phototherapy [2]. A few effective therapies exist, such as coal tar [3], but are hampered by *e.g.* displeasing odour or other side effects. Thus, there is an urgent need to find new therapeutic strategies.

Here we report the results of a clinical study on a completely new therapy for palmar psoriasis (PP) which involves the application of interferential current (IFC). This waveform is a well known tool in physiotherapy and other fields [4, 5|. Recent *in vitro* studies revealed details of its mode of action at the cellular level (see Discussion).

IFC is the most simple type of an amplitude modulated alternating current. It is usually generated by superposition ("interference") of two sinewave currents with slightly different frequencies, mostly near 4 kHz [6]. Due to the low skin impedance in the kHz-region, IFC causes no damage like burning or cauterization.

Previous clinical results based on a small case series point to 100 Hz as the most potent IFC modulation frequency for treating psoriatic plaques |7|. Meanwhile 10 Hz also proved as therapeutically effective (A. Philipp, unpublished results). Therefore, both frequencies were incorporated into the treatment concept of this study.

Since IFC application is associated with slight prickling sensations of the skin it was not possible to use a blinded study design. Therefore we conducted an open prospective study based on the hypothesis of an at least 50% response rate. Assuming a spontaneous remission rate of 18% [8], we allowed for a sufficiently large *cordon sanitaire* between expected and required rate for statistical analysis.

Patients and methods

Patients

All consecutive patients visiting our in- or outpatient-department older than 18 years with PP affecting at least 10% of the surface of both hands were eligible. Patients with pacemakers and patients with other general systemic diseases were excluded. PP was diagnosed by a senior dermatologist. The patients had been treated by other modalities before, but without success. Topical therapies were stopped two weeks, and systemic therapies including UV-treatment, 4 weeks before the start of IFC treatment. During the treatment phase, no other therapy was allowed except an ointment and lotion containing urea *(e.g.* Urea pura 10% in Ungt. leniens and Excipial-U-Lipolotio®).

Treatment modalities

The patients were treated with a commercially available IFC device operated in the bi-po3ar mode. Each patient recei-

ved his own IFC equipment and was instructed to treat his PP twice a day for 6 minutes with a modulation frequency of 100 Hz in the morning and of 10 Hz in the evening. Both sessions were separated by at least 8 hours. No ointment or lotion were allowed one hour prior to treatment. The duration of the whole therapy cycle was 12 weeks.
All patients received a standard training on the usage of the equipment. For IFC treatment, each hand was immersed in a small water-filled plastic tub. At the bottom of each tub, a 24 x 15 cm^2 rubber electrode was placed. A cellulose-cotton tissue between the electrode and the hand avoided direct electrode contact. IFC amperage was slowly upregulated by an assisting person slightly above the threshold where prickling sensation occurred, which corresponded to a typical effective current density of as low as 100 $\mu A/cm^2$.

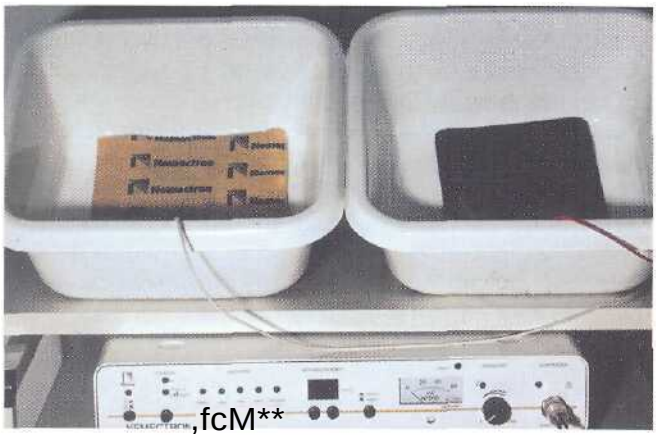

Figure 1. *The IFC equipment.*

Evaluation procedures

Based on the clinical features of the PASI (psoriasis area and severity index) score [9] we developed a clinical study score to allow for the measurement of PP severity. The overall score is the sum of the following separately recorded features: erythema, scaling, induration, fissures and pustules (0 - absent, 1 = mild, 2 - moderate, 3 = severe, 4 - extremely severe). The maximum possible value was 20 for pustular psoriasis and 16 for PP without pustules. In addition to these criteria, each patient was asked to evaluate pruritus, pain and success of the therapy by himself. These criteria were assessed every four weeks. In addition, photographs were taken. For inclusion into the study, a minimum score of 6 resp. 8 (for pustular PP) was required before therapy.

Outcome criteria

The primary outcome criteria was the clinical response, documented in a decrease of the overall score by more than 2 points. An early stopping of treatment (without complete disappearance of PP) was defined as non-response. The secondary outcome criteria were the subjective criteria as documented by the patient and were used only to validate the primary criteria.

Statistical analysis and stopping rules

As outlined in the introduction, a control group could not be formed in this study. For this group, a response rate of 18% (spontaneous remission rate) would be expected. Without a control group, a sufficient distance of safety to this null hypothesis has to be kept. Under the assumption that only a response of at least 50% would justify the application of the new therapy, it is reasonable to take a response of P_O = 50% as null hypothesis, thus creating "quasi-controlled" conditions. A binomial test against this "shifted" null hypothesis was used. In order to allow for a sufficiently high treatment efficiency, the alternative hypothesis was P1 = 80%.
The planned adaptive interim analysis [10| was performed at the time when 12 patients had been treated for twelve weeks. If $p > 0.2$, the trial would have to be stopped and the conclusion of no effect would be taken. In order to arrive at an overall significance level of a - 0.05, the significance level for the interim analysis was a' = 0.0348. Then the trial would have to be terminated and the results be judged as a significant outcome (power - 0.56). The power for not accepting the null hypothesis in the interim analysis was > 0.90. If $0.0348 < p < 0.20$, a new sample size would have to be defined in order to arrive at a statistically significant result.

Results

Patient and disease characteristics

Between October 1997 and March 1998 a total of 12 patients were included (8 men and 4 women). The mean age was 48 (36-60) years. 11 patients suffered from typical psoriasis vulgaris, three of them with deep fissures. One patient was diagnosed with pustular psoriasis. 11 patients had, in addition to the palmar involvement, typical psoriatic lesions on the trunk. All patients reported the onset of their disease more than one year ago.

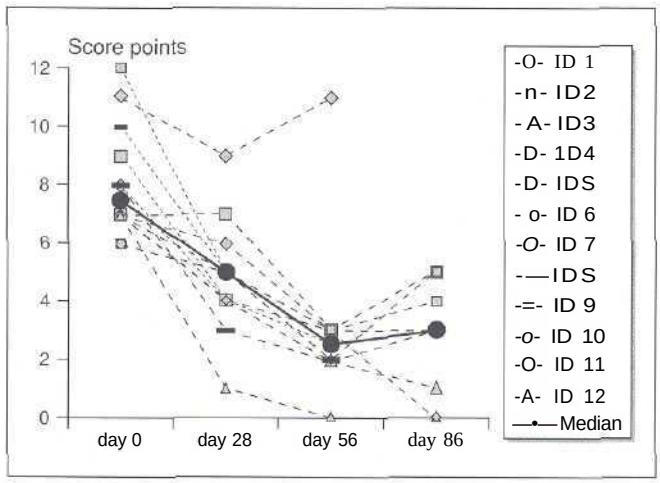

Figure 2. *Overall score and median course.*

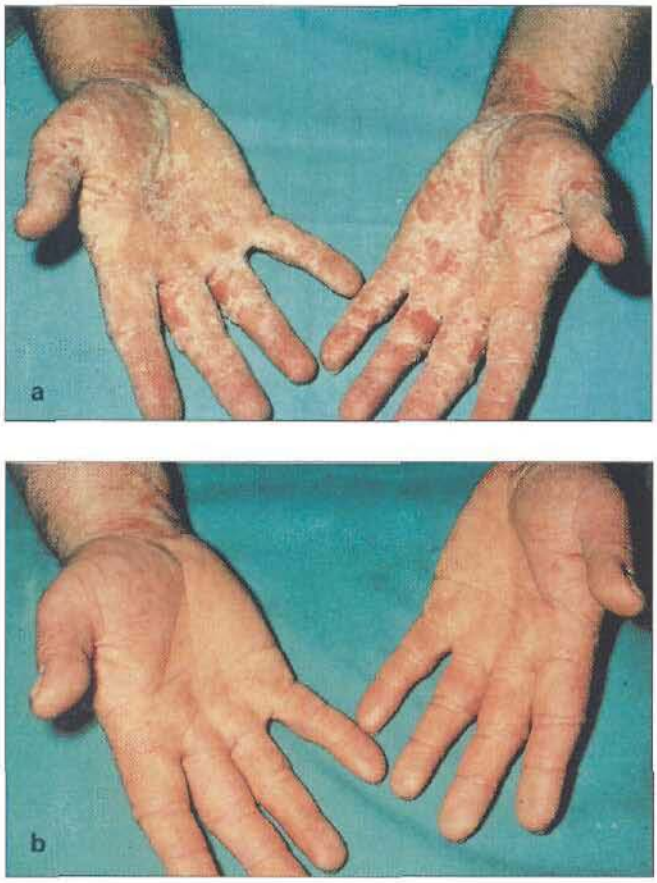

Figure 3a and b. *Patient #3 before and after 12 weeks of IFC treatment.*

Clinical response

At the end of the IFC treatment period, the overall score decreased from 7.5 (day 0) to 3.0 (day 84)
We found a decrease of the median score for erythema as well as for scaling from 3.0 points (day 0) to 1 point (day 84). The median score for induration was reduced from 2.0 points (day 0) to 1.0 point (day 84). The one patient with pustular psoriasis also showed a decrease of pustules from 3.0 (day 0) to 1.0 (day 84).
11 of 12 patients were cured or markedly improved and were considered to have demonstrated a clinical response to the therapy. Since the interim analysis indicated a significant result (p - 0.003), the trial was terminated thereafter. Estimated response rate was 90%, with a 95% confidence interval of 62 to 99%.
The subjective criteria correlated well with the objective criteria. The median of pruritus decreased from 2.0 points (day 0) to 0 points (day 84).

Discussion

We have chosen this specific study design because it allows a quasi controlled study when blinding is not possible. It requires, however, existing data on the healing rate without intervention based on previous studies on the natural history of the disease or on randomized clinical trials with a placebo group. The reader should be aware that this is a design suitable only for special conditions. It should not be done whenever a randomised clinical trial is possible.
Besides that, the planned adaptive interim analysis allows us - providing a large treatment effect exists - to control the therapy results with only a small number of patients. This was important for us for practical reasons because only 12 IFC devices were available for this study.
The results we have found reveal a high therapeutic potential of IFC in palmar psoriasis. Clinical and statistical significance was reached in an interim analysis after treatment of only 12 patients. In the study protocol the response of a patient was judged positive when the total score was reduced at least by two points after 12 weeks of treatment leading to a response rate of 90%. Even when using the criterion of a 4 points reduction of the overall score, as suggested by the median course, the response rate is still about 70%.
The clinical significance of these results is further emphasised by the following facts: (1) IFC is effective in cases where other therapies failed. Moreover, the time course of the score profile suggests that the total treatment time could eventually be reduced to 2 months. (2) No discomfort and side effects are associated with IFC treatment. Thus, additional therapy cycles can be initiated, if necessary. (3) A decrease of pruritus was reported by the patients.
Possible therapeutic mechanisms of IFC might involve activation of second messenger-dependent cell signalling processes. Specifically it has been found that the messenger cyclic AMP is upregulated in cells exposed to IFC at 10 and 100 Hz modulation [11, 12]. Also the ratio cAMP/cGMP is increased at these frequencies [12]. As shown earlier, cAMP and cAMP/cGMP, both involved in control of proliferation, are reduced in cells from psoriatic areas [13, 14]. In addition, antipsoriatic effects of dibutyryl-cAMP have been reported [!3|,
This suggests that repeated stimulation of cAMP or of cAMP/cGMP towards the normal skin values during the therapy sessions might remove psoriatic hyperproliferation. Whether or not this may explain the antipsoriatic action of IFC, will depend on the results of further investigations addressing other possible effective mechanisms, like immunological processes, but also "supportive" effects of IFC such as the stimulation of microcirculation which may influence the therapeutic result.
For the future we plan to replicate the present results on palmar psoriasis for other locations of psoriasis. In addition the combination of IFC with antipsoriatic treatments like topical vitamin-D derivates or vitamin-A will be investigated. •

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References

1.Eriksson M, Hagforsen E, Lundin I. Palmoplantar pustulosis; a clinical and immunohistological study, Br J *Dermatol* 1998; 138: 390-8.

2. Derancourt C, Van Landuyt, Laurent R. Le Psoriasis Palmo-Plantaire: diagnostic et strategie therapeutique. Ann *Dermatol Venereol* 1998; 125: 220-5.

3. Kumar B, Kumar *R,* Kaur I. Coal tar therapy in palmoplantar psoriasis: old wine in an old bottle. *Int J Dermatol* 1 997; 36: 309-12.

4. Wolf SM, Interferenzstrom-Therapie. *Elektromedizin* 1956; 1: 77-80.

5. Nikolova L. Treatment with Interferential current. Churchill Livingstone, Edinburgh-London-Melbourne-New York 1987,

6. Ward AR. Fields and Waves in Therapy, Science Press 1980; Fitzroy and Chapel Streets, Marrikville NSW 2204, Australia.

7. Wolf 6, Dertinger H, Wolf G. Die Wirkung von Interferenzstrom auf Psoriasis vulgaris. *Akt Dermatol* 1996; 22: 94-7.

8. Altmeyer PJ, Matthes U, Pawlak F, *et at.* Antipsoriatic effect of fumaric acid derivatives, *J Am Acad Dermatol* 1994; 30: 977-81.

9. Fredriksson T, Pettersson U. Severe psoriasis - oral therapy with a new retinoid. *Dermatologica* 1978; 157: 238-44.

10. Bauer P, Köhne K Evaluation of experiments with adaptive interim analyses. *Biometrics* 1994; 50:1029-41. [Correction in Biometrics 1996; 52: 380],

11. Knedlitschek G, Noszvai-Nagy M, Meyer-Waarden H, *et* al. Cyclic AMP response in cells exposed to electric fields of different frequencies and intensities. *Radiat Environ Biophys* 1994; 33: 141-7.

12. Sontag W, Dertinger H. Response of cytosolic calcium, cyclic AMP and cyclic GMP in DMSO-differentiated HL-60 cells to modulated low frequency electric currents. *Bioelectromagnetics* 1998; in press.

13. Voorhees JJ, Duell EA. Imbalanced cyclic AMP-cyclic AMP levels in psoriasis. In: *Advances in Cyclic Nucleotide Research Vol. 5* [Gl Drummond, P Greengard, GA Robinson, Eds.) 1975; Raven Press, New York, 735-58.

14. Royer E, Chaintreul J, Meynadier J, et al. Cyclic AMP and cyclic GMP productionin normal and psoriatic epidermis. *Dermatologica* 1982; 165: 533-43.

CLINICAL EFFICACY OF LOW DOSE INTERFERENTIAL CURRENTS IN THE TREATMENT OF PSORIASIS

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To date, all anti-psoriasis therapeutic regimens are not able to healing the disease permanently. The need for new treatments to reduce clinical symptoms of the chronic disease, to avoid or diminish adverse effects of conventional protocols, and to improve quality of life of the patients, fosters the research on innovative non-traditional clinical approaches including physiotherapeutic ones. We present here a clinically successful approach to the therapy of psoriasis with Interferential Currents (IFC), a wave form traditionally applied in physiotherapy. This method is based on the bipolar application of current in specific bands. A safe, pleasant, and effective treatment protocol has been developed with application of extremely low intensity IFC (approx. 50 μA/cm²) either through electrodes, covered with water-containing gel, or using electrodes placed in water baths. The procedure was performed regularly twice a day, mornings (10 Hz) and evenings (100 Hz modulation), with brief sessions of 5 minutes each. Highly positive and durable clinical effect was achieved after 8 to 12 weeks of the IFC treatment. There were no undesirable side effects, and the patients' compliance was excellent. The clinical study (Philipp et al. Eur. J. Dermatol., 2000) performed on 12 patients with therapy resistant palmar/plantar form of psoriasis, receiving local IFC treatment during a 12 weeks period, showed a 90% positive response of the patients in terms of complete remission or significant improvement of the disease. A more recent study on psoriatric arthritis (Walker et al., Rheumatol Int., 2006), on 9 patients treated for 16 weeks at affected joints, hands and feet, has demonstrated a consistent analgesic effect of the treatment, as demonstrated by the improvement of SF-36 body pain index, morning stiffness, tender joint counts, and a physician assessed disease activity.

The mechanisms of action at the molecular and cellular levels are currently obscure. However, our recent data allowed us to suggest that IFC modulated production of pro-inflammatory cytokines (IL-1β, TNF-α, and IL-10) through activation of cyclic AMP metabolic pathway affecting intracellular Ca^{+2}-transporting systems. The proliferative capacity of Th1 in response to mitogenic stimulus was substantially suppressed by IFC, which could also contribute to its anti-inflammatory effects in psoriasis.